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08/236,402	05/02/1994	RICHARD T. DEAN	DITI-107	3548

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EXAMINER
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ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 12/19/2002 44

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 08/236,402	Applicant(s) DEAN ET AL.	
	Examiner Jeffrey E. Russel	Art Unit 1654	

-- The MAILING DATE of this communication app ars on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 August 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5-8,11-17,19-21 and 34-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 5-8, 11-17, 19-21, and 34-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 May 1994* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

1. In view of the new grounds of rejection set forth below, ex parte prosecution before the examiner is resumed.

The examiner agrees with Applicants' amendment filed August 27, 2001 that claims 1-3, 5-8, 11-17, 19-21, and 34-37 are pending in this application. (At page 1, last line, of this amendment, it is believed that there is a typographical error and that "19" should instead read "19-21". It is noted that claims 20 and 21 are included in the clean copy of the claims attached with the amendment.) However, the claims as recited in the clean copy attached to the amendment contain numerous errors. For example, at claim 1, line 1, a comma should be present after "agent". At claim 1, line 2, "that" should be changed to "than". At claim 1, page 3 of the amendment, line 8, a hyphen or bond sign should be present before "H". At claim 1, page 3 of the amendment, line 10, the phrase "a sidechain group of (amino acid)[1]," should be present after the second comma. At claim 2, line 3, a comma should be present at the end of the line. At claim 36, line 3, "cause" should instead be "causes". At claim 36, line 9, the period at the end of the line should be deleted. In any amendment to the claims filed in response to this Office action, Applicants should ensure that the amendments are based upon the actual text of the claims and not upon the text of the claims as set forth in the clean copy filed August 27, 2001.

Concerning the amendment filed December 11, 1997, the amendment to page 25, line 24, was not entered because the spelling of the word "polyethyleneimine" was previously corrected by the amendment filed June 23, 1997, and because the correction proposed in the latter amendment omits "imine" from the correction.

2. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

It does not state that the person making the oath or declaration in a continuation-in-part application filed under the conditions specified in 35 U.S.C. 120 which discloses and claims subject matter in addition to that disclosed in the prior copending application, acknowledges the duty to disclose to the Office all information known to the person to be material to patentability as defined in 37 CFR 1.56 which occurred between the filing date of the prior application and the national or PCT international filing date of the continuation-in-part application.

3. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the following reasons: Amino acid sequences which are subject to the sequence disclosure rules are present, e.g., at page 12, lines 25-27 and 29; page 19, lines 15 and 16; page 20, line 35; page 21, line 2; and page 23, line 3; however, no sequence listing has been submitted. Also, SEQ ID NOS must be inserted after every amino acid sequence subject to the sequence disclosure rules. See 37 CFR 1.821(d).

Applicant must provide an original computer readable form (CRF) copy of the Sequence Listing, an original paper copy of the Sequence Listing as well as an amendment directing its entry into the specification, and a statement that the content of the paper and computer readable copies are the same and include no new matter as required by 37 CFR 1.825(a) and (b).

4. The abstract of the disclosure is objected to because of the presence of legal terminology. At line 9, "said" should be changed to "the". Correction is required. See MPEP § 608.01(b).

5. The disclosure is objected to because of the following informalities: The status of the U.S. patent applications at page 7, lines 14-15 and 17, should be updated. At page 9, line 9, "from" is misspelled. At page 20, line 20, and page 21, line 14, the beginning bracket [is unmatched. At page 21, line 12, the beginning parenthesis is unmatched. At page 24, line 21, "filed" should be changed to "field". At page 24, line 24, "acquisitions" is misspelled. Appropriate correction is required.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 34-37 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. There is no original disclosure supporting the claim limitations "metal ion-binding domain" and "radioactive metal ion" at claim 34, line 4; claim 35, lines 2-3; claim 36, line 7; and claim 37, lines 8 and 16. There is no literal support for this claim terminology in the original disclosure of the invention. In the amendment filed April 15, 1998, Appendix C, Applicants point to page 8, line 11, and page 9, lines 5 and 25-26, of the specification as support for the claim terminology. However, the claim terminology is broader in scope than either of these sections of the specification. Only a single species of metal, technetium-99m, is disclosed in the specification, which does not support claim language

directed to the entire genus of metals. Further, the original disclosure is directed to radiolabels, whereas the claim language in question does not require the metals to be radioactive. There is no original disclosure of a metal ion-binding domain which comprises Gly-Gly-Gly-Z as is recited in claims 34, 36, and 37. There is no literal support for this claim terminology in the original disclosure of the invention. In the amendment filed April 15, 1998, Appendix C, Applicants point to a nonapeptide sequence at page 12, line 27, as support for the claim terminology. However, the disclosure of a single peptide sequence consisting of nine specific amino acids does not provide support for the more generically claimed sequence which can have more than nine amino acids or as few as four amino acids and which, except for the last four amino acids, does not require any specific amino acids. Disclosure of a species does not provide written descriptive support for any and all genera encompassing the species. There is no original disclosure supporting detecting the existence or locus of inflammation as is recited in instant claim 37. There is no literal support for this claim terminology in the original disclosure of the invention. In the amendment filed April 15, 1998, Appendix C, Applicants point to page 10, lines 10-14, and Examples 2-8 of the specification as support for the new claim terminology. However, these sections of the specification do not mention inflammation.

7. Claims 7, 8, 17, and 37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. There is no antecedent basis in the claims for the phrase "the radiolabel binding moiety" at claim 7, line 2. Note that independent claim 1, line 4, uses the terminology "radiolabel complexing moiety". Claim 17 is indefinite because it requires "an effective diagnostic amount of the reagent of Claim 2". However, the reagent of claim 2 does

not comprise a radiolabel, and accordingly, it is not possible for there to be an effective amount of the unlabeled reagent. There is no antecedent basis in the claims for the phrase "the technetium-99m" at claim 17, line 3, because claim 2, upon which claim 17 depends, does not recite a radiolabeled reagent and does not recite that the reagent is complexed with technetium-99m. At claim 37, last line, the phrase "at least one of" should be inserted after "determining" so that the result of the claimed method is consistent with the preamble of the claim and so that it is clear that determining the existence and determining the locus are in the alternative to one another.

8. Claims 2, 3, and 17 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Dependent claim 2 does not further limit independent claim 1, but rather includes subject matter not embraced within the scope of the independent claim. In particular, claim 1 requires moieties of formula I to have a CO group attached to (amino acid)^1; however, this group is not recited or required in claim 2, line 3. Claim 1 requires moieties of formula II to have a NH group attached to (amino acid)^1; however, this group is not recited or required in claim 2, line 4. For moieties of formula II, claim 1 defines Y as possibly being 2-mercaptoacetate or 3-mercaptopropionate. However, claim 2, last three lines, defines the corresponding group as possibly being 2-mercaptoacetic acid or 3-mercaptopropionic acid, i.e. it specifies the free acid forms. It being possible to infringe dependent claim 2 without infringing independent claim 1, claim 2 is in improper dependent form. Claim 1 requires moieties of formula I to have a CO group attached to (amino acid)^1 and

requires moieties of formula II to have a NH group attached to (amino acid)[1]; however, these groups are not recited or required in claim 3. Accordingly, claim 3 is also in improper dependent form.

9. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-3, 5-8, 11-17, 19, and 34-36 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-37 of U.S. Patent No. 5,849,261. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the '261 patent anticipate instant claims 1-3, 5-8, 11-15, 19, and 34-36. The '261 patent claims synthetic receptor-binding VIP, which corresponds to Applicants' specific binding compound, linked to a technetium chelating moiety, which corresponds to Applicants' radiolabel complexing moiety. The '261 patent claims a technetium chelating moiety which has Applicants' formula I (see claims 15 and 18 of the '261 patent). The '261 patent claims kits for preparing the compounds, which include a reducing agent. With respect to instant claims 11-13, note that process limitations do not impart patentability to product-by-process claims where the product is otherwise anticipated by or obvious over the prior art. With respect to instant claims 12 and 16, while the '261 patent does not claim a

stannous ion reducing agent, it would have been obvious to one of ordinary skill in the art to use a stannous ion reducing agent in the claimed invention of the '261 patent because stannous ion reducing agents are routinely used in the art to prepare scintigraphic imaging agents labeled with technetium. With respect to instant claim 17, while the '261 patent does not claim a method for imaging a site, the '261 patent does claim scintigraphic imaging agents comprising radiolabeled compounds (see, e.g., claim 19), and it would have been obvious to one of ordinary skill in the art to use a claimed compound for its claimed intended purpose.

10. The effective filing date of instant claims 1-3, 5-8, 11-17, 19-21, and 34-37 is deemed to be May 2, 1994, the filing date of the instant application. The instant claims are deemed not to be entitled under 35 U.S.C. 120 to the benefit of the filing date of parent application 07/807,062 (now U.S. Patent No. 5,443,815) because the parent application, under the test of 35 U.S.C. 112, first paragraph, (1) does not disclose a molecular weight range for the specific binding compound of less than 10,000 daltons; (2) does not disclose a radiolabel complexing moiety having formula I or II; (3) does not disclose R^1 being a lower alkyl or a covalent linkage to the compound; (4) does not disclose Z linked to a NR^3R^4 group, an amino acid, or a peptide comprising 2 to 10 amino acids; (5) does not disclose R^2 being H, a lower alkyl, or a covalent linkage to the compound; (6) does not disclose Y linked to an amino acid or a peptide comprising 2 to 10 amino acids; (7) does not disclose linkage of the moiety to the compound through R^1, R^2, or a sidechain group of $(\text{amino acid})^1$ or $(\text{amino acid})^2$; (8) does not disclose the radiolabel complexing moieties of instant claim 3; (9) does not disclose a ferrous ion reducing agent as is recited in instant claims 12 and 16; (10) does not disclose a compound which binds to

a thrombus site or a site of an infection; and (11) does not disclose any of the subject matter identified in the above rejection under 35 U.S.C. 112, first paragraph.

In papers filed September 1, 1999 and April 15, 1998, Applicants have submitted arguments as to why the instant claims should be entitled to the benefit of the filing date of parent application 07/807,062. These arguments are not found to be persuasive for the following reasons: With respect to (1), while the parent application discloses peptides of between 4 and 100 amino acids, such peptides may or may not have a molecular weight of less than 10,000 daltons. There is no exact correlation between the number of amino acids and the molecular weight of a peptide. With respect to (2) and (8), the generic formulas are not described anywhere, either literally or using equivalent terminology, in the disclosure of the parent application. The disclosure in the parent application of a few peptides having specified sequences does not provide support for generic formulas encompassing the specific examples. With respect to (3) through (7), none of Applicants' citations mention these variables or compound structures. With respect to (9), claim 4 of the parent application does not recite a ferrous reducing agent. With respect to (10), the parent application does not disclose that thrombus or infection sites are sites which can be imaged (compare column 5, lines 13-30, of the parent patent). With respect to (11), the same arguments made above as to why the original disclosure of the instant application does not support the new claim limitations also apply as to why the disclosure of the parent application does not support the new claim limitations. Applicants do not provide any arguments as to how "Gly-Gly-Gly-Z" is supported by the disclosure of the parent application. In general, Applicants cite to very specific embodiments found in the disclosure of the parent application and argue that these very specific embodiments

support the more generic claim language found in the instant claims. This argument is contrary to the case law as shown by, e.g., Tronzo v. Biomet, 47 USPQ2d 1829 (Fed. Cir. 1998) and In Gosteli, 10 USPQ2d 1614 (Fed. Cir. 1989).

Note that any claim which is not directed solely to subject matter adequately disclosed in the parent application is not entitled to the benefit of the filing date of the parent application. Because the instant claims are not entitled to the benefit of the filing date of parent application 07/807,062, and because the parent application has a different inventorship than the instant application, the patent which issued based upon parent application 07/807,062 is available as prior art against the instant claims under 35 U.S.C. 102(e). This result is consistent with the statutory and case law as shown by MPEP 201.11 under "When Not Entitled To Benefit Of Filing Date", and also by Chester v. Miller, 15 USPQ2d 1333 (Fed. Cir. 1990).

On the basis of their priority claims, U.S. Patent Nos. 5,849,260 and 5,654,272 are available a prior art under 35 U.S.C. 102(e) against the instant claims regardless of whether Applicants' claims are entitled to the benefit of the filing date of parent application 07/807,062. It is noted that while U.S. Patent No. 5,849,260 is a continuation of a continuation of application serial no. 07/653,012, and U.S. Patent No. 5,654,272 is a division of the same application serial no. 07/653,012, the specifications of the two patents are not the same. Because there is at least one common inventor among this application and the two patents, and because the application and the two patents have the same assignee, Applicants are in the best position to clarify this discrepancy and make any necessary corrections. Until any such necessary corrections are made, the examiner will assume that each patent is entitled to the benefit of its earliest claimed priority date.

It should also be noted that the filing of a terminal disclaimer over a patent has no effect on rejections under 35 U.S.C. 102 or 103 based upon the availability of the patent as a prior art reference. See MPEP 804(III).

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various

claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

For the purposes of this invention, the level of ordinary skill in the art is deemed to be at least that level of skill demonstrated by the patents in the relevant art. Joy Technologies Inc. v. Quigg, 14 USPQ2d 1432 (DC DC 1990). One of ordinary skill in the art is held accountable not only for specific teachings of references, but also for inferences which those skilled in the art may reasonably be expected to draw. In re Hoeschele, 160 USPQ 809, 811 (CCPA 1969). In addition, one of ordinary skill in the art is motivated by economics to depart from the prior art to reduce costs consistent with desired product properties. In re Clinton, 188 USPQ 365, 367 (CCPA 1976); In re Thompson, 192 USPQ 275, 277 (CCPA 1976).

12. Claims 1-3, 5-8, 11-17, 19, and 34-36 are rejected under 35 U.S.C. 102(e) as being anticipated by Dean et al (U.S. Patent No. 5,443,815). Dean et al '815 teaches specific peptides in Table I which comprise a specific binding compound (e.g., the GRGD of SEQ ID NOS:2 and 3 or the RALVDTLK of SEQ ID NO:4) and a radiolabel complexing moiety (e.g., the GGC or SEQ ID NO:2 or the maGGG and PenGGG of SEQ ID NOS:3-4). The peptides are labeled with Tc-99m (see Example 2). More generally, the peptides can be labeled by incubation of the peptide in the presence of a stannous chloride reducing agent, and a kit can be provided for preparing the radiolabeled peptide by a reduction method. See, e.g., column 4, line 45 - column 5, line 5. With respect to claims 11-13, note that process limitations do not impart patentability to product-by-process claims where the product is otherwise anticipated by or obvious over the prior art. The radiolabeled peptides are used for imaging a mammalian body (see, e.g., the Abstract and column 5, lines 13-43).

13. Claims 1-3, 5-8, 11-17, 19, and 34-36 are rejected under 35 U.S.C. 102(a) as being anticipated by the WO Patent Application 93/10747. The WO Patent Application '747 contains the same disclosure as Dean et al (U.S. Patent No. 5.443,815) applied above, and anticipates the claims for the same reasons set forth above.

14. Claims 1-3, 5-8, 11-17, 19, 20, and 34-36 are rejected under 35 U.S.C. 102(e) as being anticipated by Dean et al (U.S. Patent No. 5,849,260). Dean et al '260 teaches specific peptides in the Table at columns 11-12 which comprise a specific binding compound and a radiolabel complexing moiety. The peptides are labeled with Tc-99m, either through use of a stannous chloride reducing agent or through ligand exchange, and kits for preparing the radiolabeled peptides are provided. The peptides are used to image thrombus sites in a mammalian body. See, e.g., the Abstract; column 9, lines 14-46; and Example 2. The Table teaches peptides GRGDGGC, maGGRGDF, mmpGGGRGDF, and GRGDGGGGC in which the GGC, maGG, mmpGGG, and GGGC residues, respectively, correspond to Applicants' radiolabel complexing moiety and the remaining residues correspond to Applicants' specific binding compound. Dean et al '260 also teaches, e.g., the fourth compound of the Table, in which the C-terminal GCamide residues correspond to a peptide comprising 2 amino acids attached to the carbonyl group of Applicants' Z residue, the GGGC residues correspond to Applicants' radiolabel complexing moiety of formula I, and the remainder of the compound corresponds to Applicants' specific binding compound. Note that Applicants' claims do not contain any limitations which exclude amino acids containing a thiol group from forming part of, e.g., the specific binding compound, the amino acid or peptide attached to the carbonyl group of Z, or the one or more amino acids which can link the peptide and the moiety.

15. Claims 1, 2, 5-8, 11-17, 19, and 21 are rejected under 35 U.S.C. 102(e) as being anticipated by Dean et al (U.S. Patent No. 5,561,220). Dean et al '220 teaches specific peptides at column 9, lines 21-30, and in Table I which comprise a specific binding compound and a radiolabel complexing moiety. The peptides are labeled with Tc-99m, either through use of a stannous chloride reducing agent or through ligand exchange, and kits for preparing the radiolabeled peptides are provided. The peptides are used to image inflammation and infection sites in a mammalian body. See, e.g., the Abstract; column 4, lines 41-44; and column 10, lines 4-60. With respect to the peptide, e.g., in Table I, the N-terminal AcKKKKKCG residues correspond a peptide comprising 7 amino acids linked to the amino group of Applicants' Y residue, the CGG residues correspond to Applicants' radiolabel complexing moiety of formula II, and the remaining residues correspond to Applicants' specific binding compound. Note that Applicants' claims do not contain any limitations which exclude amino acids containing a thiol group from forming part of, e.g., the specific binding compound, the amino acid or peptide attached to the amino group of Y, or the one or more amino acids which can link the peptide and the moiety.

16. Claims 1-3, 5-8, 11-17, 19, 21, and 34-37 are rejected under 35 U.S.C. 102(a) as being anticipated by the WO Patent Application 93/17719. The WO Patent Application '719 teaches specific peptides at pages 20-22 and 24 which comprise a specific binding compound and a radiolabel complexing moiety. The peptides are labeled with Tc-99m, either through use of a dithionate, stannous, or ferrous reducing agent or through ligand exchange, and kits for preparing the radiolabeled peptides are provided (see, e.g., page 14, line 24 - 15, line 6). The peptides are used to visualize sites of inflammation, including abscesses and sites of occult infection (see,

e.g., the Abstract and page 16, lines 9). With respect to the peptide, e.g., at page 20, line 17, of the WO Patent Application '719, the residues $(VGVAPG)_3$ correspond to Applicants' specific binding compound (see also page 12, line 7); the residues GGGC correspond to Applicants' radiolabel complexing moiety of formula I; and the residues GCamide correspond to a peptide comprising 2 amino acids lined to the carbonyl group of Applicants' Z.

17. Claims 1-3, 5-8, 11-17, 19, 21, and 34-37 are rejected under 35 U.S.C. 102(e) as being anticipated by Dean et al (U.S. Patent No. 6,017,510). Dean et al '510 is the U.S. equivalent of the WO Patent Application '747 applied above, and anticipates the claims for the same reasons set forth above.

18. Claims 1, 2, 5-8, 11-17, 19, and 21 are rejected under 35 U.S.C. 102(e) as being anticipated by Dean (U.S. Patent No. 5,552,525). Dean '525 teaches specific peptides in the Table at columns 10-11 which comprise a specific binding compound and a radiolabel complexing moiety. The peptides are labeled with Tc-99m, either through use of a stannous chloride reducing agent or through ligand exchange, and kits for preparing the radiolabeled peptides are provided (see, e.g., column 8, lines 21-65). The peptides are used to visualize sites of inflammation and infection (see, e.g., the Abstract and column 6, lines 52-62). With respect to the peptide, e.g., at claim 20 of Dean '525, the N-terminal residues CG correspond to a peptide comprising 2 amino acids attached to an amino group of Applicants' Y group, the residues CGG correspond to Applicants' radiolabel complexing moiety of formula II, and the remaining residues correspond to Applicants' specific binding compound (see also claim 7 of Dean '525).

19. Claims 1, 2, 5-8, 11-17, 19, and 20 are rejected under 35 U.S.C. 102(e) as being anticipated by Zamora (U.S. Patent No. 5,556,609). Zamora '609 teaches peptides comprising

the sequence YIGSR, which targets cells containing receptors for YIGSR such as platelets which occur at thrombosis sites, and also comprising a metal ion-binding domain. See, e.g., the Abstract; column 4, lines 50-64; and column 7, lines 54-63. In Example 7, the metal ion-binding domain is CDG, which corresponds to Applicants' Formula II, or GRC, which corresponds to Applicants' Formula I. In Example 7, the metal ion-binding domains are linked to the YIGSR sequences through one or more amino acids. The peptide in Example 7 labeled with Tc-99m in the presence of a stannous tartrate reducing agent. Labeling kits are also taught (see, e.g., column 7, lines 64-66). With respect to instant claim 13, process steps do not impart patentability to product-by-process claims where the product is otherwise anticipated by or obvious over the prior art.

20. Claims 1, 2, 7, 8, and 11-17 are rejected under 35 U.S.C. 102(b) as being anticipated by the WO Patent Application 89/11877. The WO Patent Application '877 teaches Tc-99m used to radiolabel 2-mercaptoacetate-Gly-Gly-Gly which is attached to a phosphate-containing targeting agent which targets calcified tissues. The radiolabeled compounds are used for detecting the presence or absence of a calcified tissue target site. Radiolabeling can occur in the presence of a reducing agent such as stannous ion, or can be the result of ligand exchange. Kits for radiolabeling are also taught. See, e.g., the Abstract; page 28, line 31 - page 30, line 18; page 34, line 16 - page 35, line 9; and claims 11 and 12.

21. Claims 1-3, 5, 19, and 34 are rejected under 35 U.S.C. 102(b) as being anticipated by the Morrison et al article (FEBS Letters, Vol. 214, pages 65-70). The Morrison et al article teaches the LHRH analog LHRH-Gly-Cys-OH, which comprises the C-terminal residues Gly-Gly-Cys. These three C-terminal residues correspond to Applicants' radiolabel complexing moiety of

formula I, and the remaining residues correspond to Applicants' specific binding compound, which in the case of the Morison et al article binds to the LHRH receptor. See, e.g., page 65.

22. Claims 1-3, 5, 6, 19, 21, and 34 are rejected under 35 U.S.C. 102(b) as being anticipated by the WO Patent Application 90/10463. The WO Patent Application '463 teaches reagents for and a method of imaging inflammation caused by infection. The reagents comprise a labeled recognition agent, where the recognition agent is capable of interacting selectively with activated leukocytes at the inflamed tissue sites. A preferred chelating compound for labeling the recognition agent is a N_3S metal chelating compound. A preferred recognition agent is a chemotactic peptide. The radiolabel can be Tc-99m. Also taught is a peptide recognition agent linked through a Gly_{1-5} spacer to a cysteine residue. Diagnostic kits including instructions for labeling are also taught. See. e.g., the Abstract; page 3, lines 7-11; page 4, line 16 - page 5, line 21; page 7, lines 3-9; page 11, line 34 - page 13, line 3; page 26, line 16 - page 27, line 3; page 38, lines 28-35; page 39, line 26 - page 41, line 5; and claims 11, 12, 17, and 29-33.

23. Claims 1, 2, 5-8, 11-17, 19, and 21 are rejected under 35 U.S.C. 103(a) as being obvious over the WO Patent Application 90/10463 as applied against claims 1-3, 5, 6, 19, 21, and 34 above, and further in view of Fritzberg et al (U.S. Patent No. 4,965,392). The WO Patent Application '463 does not teach a chemotactic peptide recognition agent labeled with N_3S metal chelating compound which is used to complex Tc-99m. Fritzberg et al '392 teaches a N_3S metal chelating compound used to label a wide variety of polypeptide and carbohydrate compounds. Fritzberg et al '392' preferred chelating compound is mercaptoacetylglycylglycylglycine, which is labeled with Tc-99m in the presence of a stannous ion reducing agent. See, e.g., column 6, line 35 - column 7, line 3; column 8, lines 24-29; and Examples I-IIIb, IV, and V. It would have

been obvious to one of ordinary skill in the art at the time Applicants' invention was made to use the mercaptoacetylglycylglycylglycine chelating compound of Fritzberg et al '392 to label the chemotactic peptide recognition agents of the WO Patent Application '463 because the mercaptoacetylglycylglycylglycine chelating compound of Fritzberg et al '392 is a species of the N_3S metal chelating compounds generically disclosed by the WO Patent Application '463, because the mercaptoacetylglycylglycylglycine chelating compound of Fritzberg et al '392 is disclosed as being useful in labeling a wide variety of polypeptide and carbohydrate compounds and therefore would have been expected to be useful in labeling the chemotactic peptide recognition agents of the WO Patent Application '463, because Fritzberg et al '392 teach that their chelating compounds have the benefit of being able to accurately direct a radionuclide to a preselected site to reduce background radiation, to reduce dosage, to minimize background for in vivo imaging, and to minimize undesirable side effects (see column 1, lines 30-38), and because Fritzberg et al '392's chelating compound would permit labeling of the WO Patent Application '463's chemotactic peptide recognition agents with Tc-99m, which the WO Patent Application '463 discloses to be a useful radionuclide.

24. Claims 1-3, 5, 6, 19, and 34 are rejected under 35 U.S.C. 102(b) as being anticipated by the Plank et al article (Bioconj. Chem., Vol. 3, pages 533-539). The Plank et al article teaches compound 1b (Figure 1), in which the C-terminal Gly-Gly-Cys residues correspond to Applicants' radiolabel complexing moiety of formula I, and the N-terminal galacotside-polylysine-Gly residues correspond to Applicants' specific binding compound, and the remaining residues correspond alternatively to portions of Applicants' radiolabel complexing

moiety, to Applicants' specific binding compound, or to the amino acids linking the peptide and the moiety. See also the Abstract.

25. Applicants' request for an interference with U.S. Patent No. 5,759,516, filed January 26, 2001, is acknowledged. Because there are currently no allowed claims in this application, it is premature to forward this application to the Board of Patent Appeals and Interferences for purposes of declaring an interference. See MPEP 2306. Further, the examiner does not agree that there is interfering subject matter between the claims of U.S. Patent No. 5,759,516, i.e. Zamora et al '516, and the claims of the instant application. Zamora et al '516, with an effective filing date of at least February 20, 1992, is deemed to be prior art against the instant claims. See the effective filing date analysis of the instant claims set forth in paragraph 10 above. However, Zamora et al '516 is not deemed to teach or suggest any of the instant claims. In particular, Zamora et al '516 does not teach or suggest a radiolabel complexing moiety having either Formula I or Formula II as set forth in independent claim 1, and does not teach or suggest any peptide comprising the partial sequence Gly-Gly-Z or Gly-Gly-Gly-Z as set forth in independent claims 34, 36, and 37. While Zamora et al '516's most general formulas (see, e.g., column 10, lines 43-46) may generically encompass Applicants' specifically claimed radiolabel complexing moieties and partial sequences, Zamora et al '516 does not provide any guidance or motivation to chose the particular amino acids which would result in Applicants' claimed invention. A disclosed genus in a prior art reference does not necessarily suggest all species encompassed by the genus. In general, see MPEP 2144.08. Accordingly, because Zamora et al '516 in general, and the claims of Zamora et al '516 in particular, do not anticipate or suggest the instant claims,

the examiner will not currently forward the application to the Board for the purposes of declaring an interference. See 37 CFR 1.607(b).

26. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (703) 308-3975. The examiner can normally be reached on Monday-Thursday from 8:30 A.M. to 6:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Brenda Brumback can be reached at (703) 306-3220. The fax number for Art Unit 1654 for formal communications is (703) 305-3014; for informal communications such as proposed amendments, the fax number (703) 746-5175 can be used. The telephone number for the Technology Center 1 receptionist is (703) 308-0196.

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November 2, 2002

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